Reviewer's report

Title: An Investigation of the Apparent Breast Cancer Epidemic in France: Screening and incidence trends in birth cohorts

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Reviewer: My von Euler-Chelpin

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Comments to the authors:
The authors have aimed at examining the relation between screening activity and incidence and mortality of breast cancer in France. They have used non-individual routine data from French registers and earlier publications.

Major comment:
There are major conceptual problems with this study. Central concepts are erroneously defined and the analyses are based on assumptions that cannot be verified:

A number of data sets were used: Mortality data (CepiDC), population data (CepiDC), cancer data (Remontet et al and the French Institute for Public Health Services), HRT data (published data), alcohol data (published data), obesity data (published data), annual number of registered mammography machines (published data) and the implementation of organised mammography screening programmes in France (reference unknown).

The authors define false positives after histology as overdiagnosis. This is rather irregular, as false-positive actually refers to the result of a test, not the diagnosis. False positive women have not been diagnosed with cancer, and should not be included among those diagnosed. Overdiagnosis is the diagnosis of cancer that, in the absence of screening, never would have become symptomatic.

In the Introduction it is unclear whether the authors actually discuss screening by mammography or diagnostic tests by use of histology, which leaves the reader confused as to the actual aim of the study.

The model for the main results is based on the assumption that there is no increase in the background incidence, except what can be attributed to three specific risk-factors, namely HRT, alcohol and obesity. There is, however, no evidence provided which explains why any residual increase immediately should be attributed to overdiagnosis.

The frequency of screening is a central concept of this study, but does not rely on participation figures or screening data, but uses the proxy of number of available mammography machines, the average use of a mammography machine in 1988, and the estimated implementation of organised screening. There is no explanation as to how these data were aggregated to show the results in Figure
On page 4, para 1 the authors state that the aim of screening is to increase global sensitivity, and therefore decreasing global specificity. The aim of screening is not to increase sensitivity, but to reduce mortality from breast cancer in the population. There is a conceptual confusion here, between the quality of the test and the aim of the intervention. Decrease in specificity does not produce overdiagnosis, but increases false-positive test results.

As a consequence of the assumptions made with regards to the background incidence, in Figure 2 the authors compare the crude incidence of breast cancer for three different years, while there should have been an estimate for breast cancer incidence in absence of screening for comparison.

As an example of a problematic definition, in Table 1 the authors indicate an increased RR of 1.17 for women taking HRT based on the 4 models in the Afssaps 2005. There is no explanation in the table or the text as to why the authors have chosen the RR for intake of estrogen+micronized progesterones for less than 5 years as their value. Although common in France they constitute only around 1/3 of the consumption in the indicated period and the RR for intake for more than 5 years is 1.53. This measure, does however, have an immediate impact on the main result.

In its present form this article does not add any substantial information to the issue of breast cancer incidence and mammography screening, as the study design does not allow the research question to be adequately answered. In view of this, other, more minor comments have not been included.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.